



## The Origin of Human Life at Fertilization: Quotes Compiled from Medical Textbooks and Peer-Reviewed Scientific Literature.<sup>1</sup>

### Note on the meaning of scientific terminology for human development:

"Organism" is the scientific name for a *living human being*. Only organisms undergo development.

"Zygote" is the one-cell human organism produced by sperm-egg fusion.

"Embryo" is a human organism during the first eight weeks of development.

### I. Medical Textbooks on Human Embryology/Reproduction

1. Keith L. Moore, *The Developing Human: Clinically Oriented Embryology*, 10th edition. Philadelphia, PA: Saunders, 2016. p. 11

“Human development begins at fertilization, when a sperm fuses with an oocyte to form a single cell, the zygote. This highly specialized, *totipotent cell* (capable of giving rise to any cell type) marks the beginning of each of us as a unique individual.”

2. Schoenwolf, G. C. *Larsen’s Human Embryology*, 5<sup>th</sup> edition. Philadelphia, PA: Elsevier, Saunders, 2015. p. 2, 14.

“All of us were once human embryos, so the study of human embryology is the study of our own prenatal origins and experiences.” (p. 2)

“Fertilization, the uniting of egg and sperm, takes place in the oviduct. After the oocyte finishes meiosis, the paternal and maternal chromosomes come together, resulting in the formation of a zygote containing a single diploid

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nucleus. Embryonic development is considered to begin at this point."  
(p.14)

3. Jones, R. E. **Human Reproductive Biology**, 4<sup>th</sup> edition. Waltham, MA. Elsevier, Academic Press, 2014, p. 169.

"the fertilized egg (zygote) is the beginning of a new diploid individual."

4. Keith L. Moore, **Before We Are Born: Essentials of Embryology**, 7th edition. Philadelphia, PA: Saunders, 2008. p. 2:

"[The zygote], formed by the union of an oocyte and a sperm, is the beginning of a new human being."

5. Keith L. Moore, **Before We Are Born: Essentials of Embryology**, 9th edition. Philadelphia, PA: Saunders, 2016. p. 1.

"Human development begins at fertilization when an oocyte (ovum) from a female is fertilized by a sperm (spermatozoon) from a male...Embryology is concerned with the origin and development of a human being from a zygote to birth."

6. Sadler, T. W. **Langman's Medical Embryology**, 10th edition. Philadelphia, PA: Lippincott Williams & Wilkins, 2006. p. 11:

"Development begins with fertilization, the process by which the male gamete, the sperm, and the female gamete, the oocyte, unite to give rise to a zygote."

7. Sadler, T. W. **Langman's Medical Embryology**, 13th edition. Philadelphia, PA: Lippincott Williams & Wilkins, 2015. p. 42 (*emphasis added*).

"The main results of fertilization are as follows: Restoration of the diploid number of chromosomes, half from the father half from the mother. Hence, the zygote contains a new combination of chromosomes different from both parents. Determination of the sex of the new individual. An X-carrying sperm produces a female (XX) embryo and a Y-carrying sperm produces a male (XY) embryo. Therefore, the chromosomal sex of the embryo is determined at fertilization."

8. Dudek, R. W. *Embryology*, 4<sup>th</sup> edition. Philadelphia, PA. Lippincott Williams and Wilkins, 2008, p. 1.

“Sexual reproduction occurs when female and male gametes (oocyte and spermatozoon, respectively) unite at fertilization.”

9. Ronan O’Rahilly and Fabiola Miller, *Human Embryology and Teratology*, 3rd edition. New York: Wiley-Liss, 2001. p. 8.

“Although life is a continuous process, fertilization... is a critical landmark because, under ordinary circumstances, a new genetically distinct human organism is formed when the chromosomes of the male and female pronuclei blend in the oocyte.”

10. Carlson, B. M. *Human Embryology and Developmental Biology*, 5<sup>th</sup> edition. Philadelphia, PA. Elsevier, Saunders, 2014, p. 2.

“Human pregnancy begins with the fusion of an egg and a sperm within the female reproductive tract.”

## II. Peer-reviewed scientific literature (2001-present)(chron. order)

1. A profile of fertilization in mammals. Wassarman PM, Jovine L, Litscher ES. Nat Cell Biol. 2001.3(2):E59-64.

“When mammalian eggs and sperm come into contact in the female oviduct, a series of steps is set in motion that can lead to fertilization and ultimately to development of new individuals.”

2. Penetration, adhesion, and fusion in mammalian sperm-egg interaction. Primakoff P, Myles DG. Science. 2002. 296(5576):2183-5.

“Fertilization is the sum of the cellular mechanisms that pass the genome from one generation to the next and initiate development of a new organism.”

3. Egg activation at fertilization: where it all begins. Runft LL, Jaffe LA, Mehlmann LM. Dev Biol. 2002. 245(2):237-54.

4. The cell cycle: a new entry in the field of Ca<sup>2+</sup> signaling. Santella L, Ercolano E, Nusco GA. *Cell Mol Life Sci.* 2005. 62(21):2405-13.

“Ca<sup>2+</sup> signaling plays a crucial role in virtually all cellular processes, from the origin of new life at fertilization to the end of life when cells die.”

5. The immunoglobulin superfamily protein Izumo is required for sperm to fuse with eggs. Inoue N, Ikawa M, Isotani A, Okabe M. *Nature.* 2005. 434(7030):234-8.

“Representing the 60 trillion cells that build a human body, a sperm and an egg meet, recognize each other, and fuse to form a new generation of life.”

6. Signal transduction pathways leading to Ca<sup>2+</sup> release in a vertebrate model system: lessons from *Xenopus* eggs. Sato K, Fukami Y, Stith BJ. *Semin Cell Dev Biol.* 2006. 17(2):285-92.

“At fertilization, eggs unite with sperm to initiate developmental programs that give rise to development of the embryo. Defining the molecular mechanism of this fundamental process at the beginning of life has been a key question in cell and developmental biology.”

7. Cell fusion during development. Oren-Suissa M, Podbilewicz B. *Trends Cell Biol.* 2007. 17(11):537-46.

“Most readers of this review originated from a sperm-egg fusion event.”

8. Ca<sup>2+</sup> signaling differentiation during oocyte maturation. Machaca K. *J Cell Physiol.* 2007. 213(2):331-40.

“Oocyte maturation is an essential cellular differentiation pathway that prepares the egg for activation at fertilization leading to the initiation of embryogenesis.”

9. Sperm-egg fusion assay in mammals. Inoue N, Okabe M. *Methods Mol Biol.* 2008. 475:335-45.

“As representatives of the 60 trillion cells that make a human body, a sperm and an egg meet, recognize each other, and fuse to create a new generation.”

10. Sperm chromatin: fertile grounds for proteomic discovery of clinical tools. Wu TF, Chu DS. Mol Cell Proteomics. 2008. 7(10):1876-86.

“Sperm are remarkably complex cells with a singularly important mission: to deliver paternal DNA and its associated factors to the oocyte to start a new life.”

11. Gene expression during the oocyte-to-embryo transition in mammals. Evsikov AV, Marín de Evsikova C. Mol Reprod Dev. 2009. 76(9):805-18.

“The seminal question in modern developmental biology is the origins of new life arising from the unification of sperm and egg.”

12. A role for the elongator complex in zygotic paternal genome demethylation. Okada Y, Yamagata K, Hong K, Wakayama T, Zhang Y. Nature. 2010. 463(7280):554-8.

“The life cycle of mammals begins when a sperm enters an egg.”

13. Fertilization and the oocyte-to-embryo transition in *C. elegans*. Marcello MR, Singson A. BMB Rep. 2010. 43(6):389-99.

“Fertilization is a complex process comprised of numerous steps. During fertilization, two highly specialized and differentiated cells (sperm and egg) fuse and subsequently trigger the development of an embryo from a quiescent, arrested oocyte.”

14. Model systems for membrane fusion. Marsden HR, Tomatsu I, Kros A. Chem Soc Rev. 2011. 40(3):1572-85.

“The fusion of sperm and egg membranes initiates the life of a sexually reproducing organism.”

15. Calcium channels in the development, maturation, and function of spermatozoa. Darszon A, Nishigaki T, Beltran C, Treviño CL. Physiol Rev. 2011. 91(4):1305-55.

“A proper dialogue between spermatozoa and the egg is essential for conception of a new individual in sexually reproducing animals. Ca<sup>2+</sup> is crucial in orchestrating this unique event leading to a new life.”

16. Acrosome reaction in the cumulus oophorus revisited: involvement of a novel sperm-released factor NYD-SP8. Sun TT, Chung CM, Chan HC. Protein Cell. 2011. 2(2):92-8.

“Fertilization is a process involving multiple steps that lead to the final fusion of one sperm and oocyte to form the zygote.”

17. Starting a new life: sperm PLC-zeta mobilizes the Ca<sup>2+</sup> signal that induces egg activation and embryo development: an essential phospholipase C with implications for male infertility. Nomikos M, Swann K, Lai FA. Bioessays. 2012. 34(2):126-34.

18. Kinases, phosphatases and proteases during sperm capacitation. Signorelli J, Diaz ES, Morales P. Cell Tissue Res. 2012. 349(3):765-82.

“Fertilization is the process by which male and female haploid gametes (sperm and egg) unite to produce a genetically distinct individual.”

19. Roles of the oviduct in mammalian fertilization. Coy P, Garcia-Vázquez FA, Visconti PE, Avilés M. Reproduction. 2012. 144(6):649-60.

“The oviduct or Fallopian tube is the anatomical region where every new life begins in mammalian species. After a long journey, the spermatozoa meet the oocyte in the specific site of the oviduct named ampulla, and fertilization takes place.”

20. Oviductal, endometrial and embryonic gene expression patterns as molecular clues for pregnancy establishment. Salilew-Wondim D, Schellander K, Hoelker M, Tesfaye D. Anim Reprod Sci. 2012. 134(1-2):9-18.

“In higher animals, the beginning of new life and transfer of genetic material to the next generation occurs in the oviduct when two distinct gametes cells unite resulting in the formation of a zygote.”

21. Sperm-egg interaction. Evans JP. Annu Rev Physiol. 2012. 74:477-502.

“A crucial step of fertilization is the sperm-egg interaction that allows the two gametes to fuse and create the zygote.”

- 22.Regulation of inositol 1,4,5-trisphosphate receptor function during mouse oocyte maturation. Wakai T, Vanderheyden V, Yoon SY, Cheon B, Zhang N, Parys JB, Fissore RA. J Cell Physiol. 2012. 227(2):705-17.

“At the time of fertilization, an increase in the intracellular Ca(2+) concentration ([Ca(2+)](i)) underlies egg activation and initiation of development in all species studied to date.”

- 23.Fertilization. Marcello MR, Singaravelu G, Singson A. Adv Exp Med Biol. 2013. 757:321-50.

“Fertilization-the fusion of gametes to produce a new organism-is the culmination of a multitude of intricately regulated cellular processes.”

- 24.The oocyte-to-embryo transition. Robertson S, Lin R. Adv Exp Med Biol. 2013. 757:351-72.

"The oocyte-to-embryo transition refers to the process whereby a fully grown, relatively quiescent oocyte undergoes maturation, fertilization, and is converted into a developmentally active, mitotically dividing embryo, arguably one of the most dramatic transitions in biology."

- 25.How to make a good egg!: The need for remodeling of oocyte Ca(2+) signaling to mediate the egg-to-embryo transition. Nader N, Kulkarni RP, Dib M, Machaca K. Cell Calcium. 2013. 53(1):41-54.

“The egg-to-embryo transition marks the initiation of multicellular organismal development and is mediated by a specialized Ca(2+) transient at fertilization.”

- 26.Membrane rafts regulate phospholipase B activation in murine sperm. Asano A, Nelson-Harrington JL, Travis AJ. Commun Integr Biol. 2013. 6(6):e27362.

“It is intuitive that fertilization-the start of life-involves communication between a sperm cell and an egg.”

27. Juno is the egg Izumo receptor and is essential for mammalian fertilization. Bianchi E, Doe B, Goulding D, Wright GJ. *Nature*. 2014. 508(7497):483-7.

“Fertilization occurs when *sperm and egg recognize each other and fuse to form a new, genetically distinct organism.*”

28. A transgenic insertion on mouse chromosome 17 inactivates a novel immunoglobulin superfamily gene potentially involved in sperm-egg fusion. Lorenzetti D, Poirier C, Zhao M, Overbeek PA, Harrison W, Bishop CE. *Mamm Genome*. 2014. 25(3-4):141-8.

“Fertilization is the process that *leads to the formation of a diploid zygote* from two haploid gametes.”

29. MicroRNA-34 family expression in bovine gametes and preimplantation embryos. Tscherner A, Gilchrist G, Smith N, Blondin P, Gillis D, LaMarre J. *Reprod Biol Endocrinol*. 2014. 12:85.

“In sexually reproducing organisms, *embryogenesis begins with the fusion of two haploid gametes.*”

30. Cross-species fertilization: the hamster egg receptor, Juno, binds the human sperm ligand, Izumo1. Bianchi E, Wright GJ. *Philos Trans R Soc Lond B Biol Sci*. 2015. 370(1661):20140101.

“Fertilization is the culminating event in sexual reproduction and requires the recognition and *fusion of the haploid sperm and egg to form a new diploid organism.*”

31. Maternal non-Mendelian inheritance of a reduced lifespan? A hypothesis. Wilding M, Coppola G, De Icco F, Arenare L, Di Matteo L, Dale B. *J Assist Reprod Genet*. 2014. 31(6):637-43.

“Since *a new individual is derived from the fusion of a single sperm and egg, we tested...*”

32. An update on post-ejaculatory remodeling of the sperm surface before mammalian fertilization. Gadella BM, Boerke A. *Theriogenology*. 2015. 85(1):113-24.



*“The fusion of a sperm with an oocyte to form new life is a highly regulated event.”*

33. PLC $\zeta$  or PAWP: revisiting the putative mammalian sperm factor that triggers egg activation and embryogenesis. Kashir J, Nomikos M, Swann K, Lai FA. Mol Hum Reprod. 2015. 21(5):383-8.

*“In mammals, egg activation is initiated by multiple cytosolic Ca(2+) transients (Ca(2+) oscillations) that are triggered following delivery of a putative sperm factor from the fertilizing sperm. The identity of this 'sperm factor' thus holds much significance, not only as a vital component in creating a new life, but also for its potential therapeutic and diagnostic value in human infertility.”*

34. 2015 RANZCOG Arthur Wilson Memorial Oration 'From little things, big things grow: The importance of periconception medicine'. Norman RJ. Aust N Z J Obstet Gynaecol. 2015. 55(6):535-40.

*“The time of our conception is when we are most vulnerable to survival and growing as a healthy human being.”*

35. State of the art in cell-cell fusion. Willkomm L, Bloch W. Methods Mol Biol. 2015. 1313:1-

*“Mammalian life begins with a cell-cell fusion event, i.e. the fusion of the spermatozoid with the oocyte”*

36. Mapping the journey from totipotency to lineage specification in the mouse embryo. Leung CY, Zernicka-Goetz M. Curr Opin Genet Dev. 2015. 34:71-6.

*“Mammalian life, with all its complexity comes from a humble beginning of a single fertilized egg cell.”*

37. The anaphase-promoting complex initiates zygote division in Arabidopsis through degradation of cyclin B1. Guo L, Jiang L, Zhang Y, Lu XL, Xie Q, Weijers D, Liu CM. Plant J. 2016. 86(2):161-74.

*“As the start of a new life cycle, activation of the first division of the zygote is a critical event in both plants and animals.”*

38. The role of syncytins in human reproduction and reproductive organ cancers. Soygur B, Sati L. *Reproduction*. 2016. 152(5):R167-78.

*“Human life begins with sperm and oocyte fusion.”*

39. Parental Control Begins at the Beginning. Chu D. *Genetics*. 2016. 204(4):1377-1378.

*“New parents anticipate their job begins at birth. Little do they know they have been exerting control within the baby’s first cell since fertilization.”*

40. Meiotic Divisions: No Place for Gender Equality. El Yakoubi W, Wassmann K. *Adv Exp Med Biol*. 2017. 1002:1-17.

*“In multicellular organisms the fusion of two gametes with a haploid set of chromosomes leads to the formation of the zygote, the first cell of the embryo.”*

41. Signal transduction in mammalian oocytes during fertilization. Machaty Z. *Cell Tissue Res*. 2016. 363(1):169-83.

*“Mammalian embryo development begins when the fertilizing sperm triggers a series of elevations in the oocyte's intracellular free Ca(2+) concentration.”*

42. ZYGOTE-ARREST 3 that encodes the tRNA ligase is essential for zygote division in Arabidopsis. Yang KJ, Guo L, Hou XL, Gong HQ, Liu CM. *J Integr Plant Biol*. 2017. 59(9):680-692.

*“In sexual organisms, division of the zygote initiates a new life cycle.”*

43. *When sperm meets egg: the spark of new life.* Wozniak KL, Luque GM, Ahn SH. *Mol Reprod Dev*. 2017. doi: 10.1002/mrd.22857. [Epub ahead of print]

44. Histone 3 lysine 9 acetylation is a biomarker of the effects of culture on zygotes. Rollo C, Li Y, Jin XL, O'Neill C. *Reproduction*. 2017. 154(4):375-385.

*“Fertilisation triggers a round of chromatin remodelling that prepares the genome for the first round of transcription from the new embryonic genome.”*

45. Hutchinson-Gilford Progeria Syndrome: A Premature Aging Disease. Ahmed MS, Ikram S, Bibi N, Mir A. Mol Neurobiol. 2017. doi: 10.1007/s12035-017-0610-7. [Epub ahead of print]

“Aging is a developmental process that begins with fertilization and ends up with death involving a lot of environmental and genetic factors.”

46. Egg Activation at Fertilization. Machaty Z, Miller AR, Zhang L. Adv Exp Med Biol. 2017. 953:1-47.

“Fertilization is the union of gametes to initiate development of a new individual.”

47. LINE-1 activation after fertilization regulates global chromatin accessibility in the early mouse embryo. Jachowicz JW, Bing X, Pontabry J, Bošković A, Rando OJ, Torres-Padilla ME. Nat Genet. 2017. 49(10):1502-1510.

[referring to events in the zygote] “Our data suggest that activation of LINE-1 regulates global chromatin accessibility at the beginning of development and indicate that retrotransposon activation is integral to the developmental program.”

48. “This is where it all started” - the pivotal role of PLC $\zeta$  within the sophisticated process of mammalian reproduction: a systemic review. Gat I, Orvieto R. Basic Clin Androl. 2017. 21;27:9.

“At the end of oogenesis and spermatogenesis, both haploid gametes contain a single set of chromosomes ready to form the zygote, the first cell of the newly developing individual.”

49. Epigenetic modifications and reprogramming in paternal pronucleus: sperm, preimplantation embryo, and beyond. Okada Y, Yamaguchi K. Cell Mol Life Sci. 2017. 74(11):1957-1967.

“Pronuclear/zygotic stage is the very first stage of life.”

50. PLC $\zeta$  is the physiological trigger of the Ca<sup>2+</sup> oscillations that induce embryogenesis in mammals but conception can occur in its absence. Hachem A, Godwin J, Ruas M, Lee HC, Ferrer Buitrago M, Ardestani G, Bassett A, Fox S,

Navarrete F, de Sutter P, Heindryckx B, Fissore R, Parrington J. Development. 2017. 144(16):2914-2924.

*“Activation of the egg by the sperm is the first, vital stage of embryogenesis.”*

51. Structural Basis of Egg Coat-Sperm Recognition at Fertilization. Raj I, Sadat Al Hosseini H, Dioguardi E, Nishimura K, Han L, Villa A, de Sanctis D, Jovine L. Cell. 2017. 169(7):1315-1326.e17.

*“Recognition between sperm and the egg surface marks the beginning of life in all sexually reproducing organisms.”*

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